



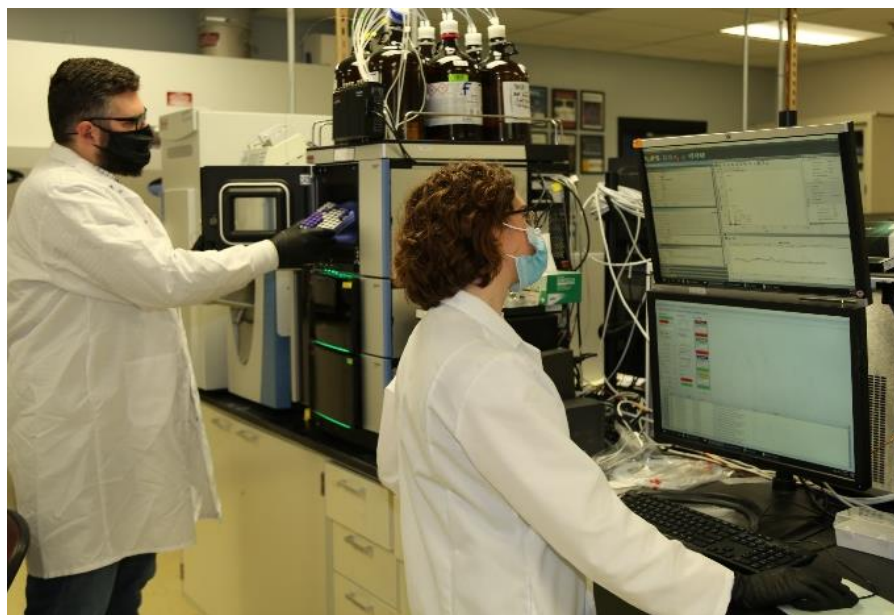
The Combat Capabilities Development Command (DEVCOM) Chemical Biological Center, formerly known as the U.S. Army Edgewood Chemical Biological Center, is the Army's principal research and development center for chemical and biological defense technology, engineering and field operations. The headquarters of the CCDC Chemical Biological Center is located at the Edgewood Area of Aberdeen Proving Ground, Maryland.

For Information: Richard Arndt, 410-436-1479

5 May 2021

## Army Scientists Find New Potential Counter to Nerve Agent Exposure

*By Dr. Brian B. Feeney*



*DEVCOM Chemical Biological Center research scientist Dr. Phillip Mach loads prepared blood samples into a liquid chromatography auto-sampler while Dr. Elizabeth Dhummakupt prepares the system for analyzing the samples.*

**Aberdeen Proving Ground, MD --** When it comes to the nerve agent VX, even a tiny drop on the skin is quickly fatal. Army researchers at the Combat Capabilities Development Command Chemical Biological Center are now busy developing a way to counteract the way VX attacks life-sustaining molecular activities inside human cells, and they are doing it using a common, over-the-counter nutritional supplement.

"We already have a way to stop one of two ways in which VX kills you," said Dr. Phillip Mach, a Center research scientist. "The first way by blocking the substance that breaks the neuro transmitter to the muscles that tells a person to breathe. If that neural bridge isn't broken, the muscles can't ever stop flexing and relax, so breathing stops. We can stop VX from doing that by giving warfighters an auto-injector containing a medical counter measure.

"The second way is for VX to stop the complex energy production system inside human cells, which most people know as the citric acid cycle from college biology."

Midway through the citric acid cycle the body creates alpha-Ketoglutarate. When VX inhibits its production the body stops producing energy, quickly causing death. Mach and his research partner at the Center, Dr. Elizabeth Dhummakupt, discovered this



# News Release

<https://cbc.ccdc.army.mil>

phenomenon while doing unrelated VX exposure research on interstitial fluid. Interstitial fluid is the bodily fluid between blood vessels and cells, much like a liquid packing material inside the body. It mirrors the blood in the body and constantly changes in response to what the body is doing, just like blood. Also, just like blood, it changes with a person's daily activities, such as exercise and dietary habits.

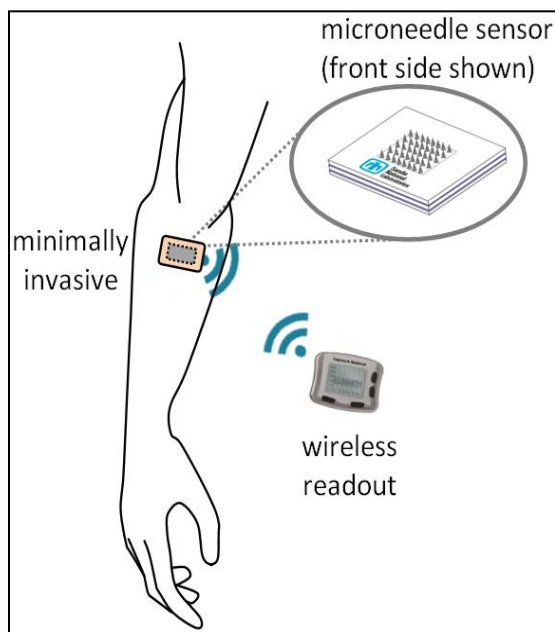
They noticed that after VX exposure in laboratory samples, the interstitial fluid's proteins showed a marked change, and the proteins related to energy production changed the most. Alpha-Ketoglutarate was one of them. Mach and Dhummakupt decided they needed to know more.

They discussed this unexpected observation with their colleagues in the Center's Toxicology Branch and learned that this group had done a lot of research on how VX affects the heart. They had even developed a method for placing heart cells on a chip to closely monitor VX's effects on heartbeat.

Mach, Dhummakupt and the rest of their team started by mapping out the citric acid cycle on a whiteboard. Next, they performed time studies on VX-exposed heart cells on a chip and were able to pinpoint the moment that energy production stopped – just when alpha-Ketoglutarate, known as  $\alpha$ KG, was supposed to be formed inside the heart cells. It just so happens that  $\alpha$ KG is also a popular nutrition supplement that can be purchased at nutrition stores everywhere. So why not try injecting a tiny bit of  $\alpha$ KG into the heart cells on a chip as soon as they become stricken? They did, and the cells immediately resumed energy production. "It seemed too easy," said Dhummakupt. "How could this not already be known and published?"

There were several reasons why. First, the instruments and software needed to do that kind of time lapse observation of cells has only recently been developed. But more fundamentally, discovering this type of highly-specialized information requires a laser-like focus on chemical warfare agent exposure.

Their next question was, "How do we turn this discovery into something that can benefit the warfighter?" Their minds turned to smartwatches that can continuously monitor athletes' vital functions while they train. They also thought about glucose monitors for diabetics. If the glucose level is severely elevated, a smartphone containing a glucose sensor will not only identify it, but will also automatically call the doctor.



*A microneedle patch placed on a warfighter's skin can provide continuous monitoring of interstitial fluid and if proteins characteristic of nerve agent exposure is detected, it can send an auto-alert.*



# News Release

<https://cbc.ccdc.army.mil>

They decided they could place a microneedle patch on the skin of a warfighter as a wearable sensor that can provide a wireless readout to a command and control module. The micro needles access the interstitial fluid close to the skin and determine whether or not proteins characteristic of VX exposure are present.

“At first we wondered if it might be uncomfortable, but we found out that the sensation of the patch is more like the minor scratchiness of sandpaper,” said Mach. “The idea is that if an exposure is detected, the warfighter can simply pull some αKG pills out of his or her pocket and swallow them. Another possibility, if an area may be hot, is to just take the pills beforehand. We want to prove this through further research.”

With the concept proven, the next step for Mach and Dhummakupt is to determine just the right dosage of αKG by working with other defense research laboratories that specialize in medical countermeasures to chemical warfare agents.

“It’s always nice to get the benefit of some serendipity while doing this kind of research, now we are going to be able to really make a difference by making warfighters more safe in the field,” said Mach.

###30###

For more information about the CCDC Chemical Biological Center, visit <https://cbc.ccdc.army.mil>